REMARKS

Claims 1-27 are pending and under consideration in the above-identified application. Claims 28-59 have been cancelled previously without prejudice.

Claims 17 and 21 have been amended to indicate with greater clarity that the claims are directed to compositions rather than processes. The amendments add no new matter and are believed to place the application in better condition for allowance. Accordingly, entry of the amendments is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

A. Written Description

The rejection of claims 1-27 under 35 U.S.C. § 112, first paragraph, for allegedly failing to provide adequate written description of the invention is respectfully traversed.

Independent claim 1 is directed to a composition of compounds effective for treating a pathology, the composition that includes a combination of at least two compounds that modulate the activity of one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs), wherein each compound modulates the activity of at least one target molecule associated with one or more SNPs, and wherein the combination is effective for at least one patient having the pathology.

Independent claim 20 is directed at a composition of compounds effective for treating a pathology, said composition comprising at least two compounds that modulate the activity of at least one target molecule associated with at least one SNP, wherein said combination is effective for at least one patient having said pathology.

The Office Action asserts that Applicant has not exemplified a composition having each of the elements of the claimed invention (current Office Action, page 7, second paragraph). It is further alleged that the disclosure of five compounds in the

specification is not representative of the claimed genus of a composition encompassing 2 compounds that modulate the activity of any SNP, to levels that the combination of compounds effectively treats at least 90% of patients having the pathology (current Office Action, paragraph bridging pages 7 and 8). The Office Action cites *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991) and *Regents of University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir.1997) to support the assertion that Applicant has not identified a representative number of compounds within the claimed genus. Applicant respectfully disagrees with the Examiner's characterization of the written description case law and maintains that the specification provides adequate written description of the claimed invention.

The written description requirement of § 112 does not require that a patent specification sets forth in a single embodiment all of the steps of a claimed invention. To the contrary, the Federal Circuit has held that

> [t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.' . . . Thus, § 112, paragraph 1 ensures that, as of the filing date, the inventor conveyed with reasonable clarity to those of skill in the art that he was in possession of the subject matter of the claims.

Union Oil Co. of Cal. v. Atl. Richfield Co., 208 F.3d 989, 997 (Fed. Cir. 2000) (quoting *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989)).

This is consistent with the well-established legal principle that claims are not limited to the specific embodiments disclosed in the specification. See *Renishaw PLC v. Marposs Societá per Azioni*, 158 F.3d 1243, 1249 (Fed. Cir. 1998). An accused infringer cannot narrow the scope of a claim "simply by pointing to the preferred embodiment or other structures or steps disclosed in the specification . . . ." *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002) ("our case law makes clear that a patentee need not 'describe in the specification every conceivable and possible future embodiment of his invention'"); see also *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1121 (Fed. Cir. 1985). "'A specification may, within the meaning of 35

U.S.C. § 112, paragraph 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.'" E.g., *Vas-Cath*, 935 F.2d at 1563 n.6 (quoting *Kennecott Corp. v. Kyocera Int'l, Inc.*, 835 F.2d 1419 (Fed. Cir. 1987)); *Xerox Corp. v. 3Com Corp.*, 198 F. Supp. 2d 283, 297 (W.D.N.Y. 2001)

The Federal Circuit also has indicated that a rejection for lack of written description is appropriate where the claims cannot be practiced based on the specification, even considering the knowledge of one skilled in the art. *See, University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927 (2004). In *Rochester*, the Federal Circuit recently indicated that the issue for written description is not simply whether claimed compounds are disclosed, but also whether such claimed compound were known in the art. *See Id.*

Applicant respectfully submits that the skilled person with knowledge of the art and familiar with the specification, would be able to select art-known compounds suitable for inclusion in a composition of the invention. The specification provides written description to the skilled person by teaching that a compound that is effective against a target molecule associated with one or more particular genetic variations modulates the activity of a target molecule that plays a role in the symptoms, etiology, complications or treatment of a pathology (specification, page 7, lines 8-14). Significantly, such compounds suitable for inclusion in the claimed compositions were known in the art and the skilled person familiar with the specification would have known of such compounds. A specification need not describe—and best omits—that which is well known in the art. See, e.g., *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991).

The specification describes compounds suitable for inclusion in a composition of the invention by indicating that the term is used in reference to a pharmaceutically active agent used to effect a physiological change in treating a pathology (specification, page 4, lines 17-23)). The specification teaches that exemplary compounds can be chosen from drugs, pharmaceutically active natural products or dietary supplements, or any other type of compound useful in treating a pathology (specification, page 4, lines 24-27). It is further described that, preferably, one or more of the compounds in the composition will

be targeted toward treating a subset of the total population of patients with a pathology, in which the constituents of this subset have related or identical genetic profiles (specification, page 4, lines 27-31). The specification also describes an invention composition of compounds as preferably including specific amounts of two or more compounds, combined for the purpose of effectively treating an optimum percentage of patients with a pathology while maintaining little or no toxicity. Applicant respectfully submits that the skilled person with knowledge of the art and familiar with the specification, would be able to select art-known compounds suitable for inclusion in a composition of the invention. In particular, the skilled artisan familiar with the specification, would be able to envision compounds suitable for inclusion in a composition of the invention, for example, a drug, pharmaceutically active natural product or dietary supplement known to be useful in treating a pathology.

Accordingly, Applicant respectfully requests removal of the rejection of claims 1-27 under 35 U.S.C. § 112, first paragraph, for allegedly failing to provide adequate written description of the invention.

B. Regarding Enablement

The independent rejection of claims 1-27 under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification so as to enable one skilled in the art to practice the claimed invention also is traversed.

The Office Action maintains that, while enabling for compositions consisting of a specific HIV vaccine of U.S. Patent No. 5,846,546, and the HBV antibody composition of U.S. Patent No. 5,648,077, the specification does not reasonably provide enablement for compositions containing two or more compounds that are to be used to treat any pathology, wherein the compounds modulate the activity of one or more target compounds associated with any SNP (current Office Action, page 8, second paragraph). In response to Applicant's submission of publications that clearly demonstrate that the identification of a target molecule that is associated with one or more SNPs that plays a role in the symptoms, etiology, complications or treatment of a pathology were known in

the art at the time the present application was filed, the Office Action concedes that the prior art teaches compounds that modulate the activity of a SNP, but argues that such teachings directed to specific SNPs associated with specific diseases are not sufficient to support the enablement of the claimed invention of any combination of compounds that modulate in any manner any SNP present in any gene and associated with any pathology. The Office Action asserts that the experimentation required to identify the compounds present in the claimed compositions is extensive and highly unpredictable and would not be considered by the artisan to be routine.

Applicant submits that any use that reasonably correlates with the scope of the claim is sufficient to preclude a rejection for nonenablement based on how to use. In *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998), the Federal Circuit clearly stated that routine experimentation does not constitute undue experimentation:

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Id. (Emphasis added) (citing *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d at 1564, 37 U.S.P.Q.2d at 1623); see also *In re Wands*, 858 F.2d at 736-40, 8 U.S.P.Q.2d at 1403-07.

"The law does not require a specification to be a blueprint in order to satisfy the enablement requirement," *Staehelin v. Secher*, 24 U.S.P.Q. 2d 11513, 1516 (Bd. Pat. App. & Int. 1992). A specification need not describe—and best omits—that which is well known in the art. See, e.g., *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991). It is also well-settled in the law that "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the

experimentation should proceed." *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. App. 1982).

Even in the relatively "unpredictable" arts, one need not necessarily disclose how to make each and every embodiment encompassed by the claim. For example, in *In re Angstadt*, 537 F.2d 498, 190 U.S.P.Q. 214 (C.C.P.A. 1976), the court noted that some experimentation is often to be expected in unpredictable areas of technologies. The court further observed that if § 112 required a disclosure of a test with every species covered by a claim in an unpredictable art, then a prohibited number of actual experiments would have to be performed, discouraging the filing of patent applications in unpredictable areas. Id.

Briefly, a component compound of a composition of the invention modulates a target molecule associated with one or more SNPs. For a particular pathology, one or more SNPs can be correlated with the symptoms, etiology, side-effects or progression of treatment of that pathology as well as with the efficacy, or toxicity, or both, of a compound used for treating the pathology (specification as filed, page 9, lines 3-9). Patients with a particular pathology have a unique combination of genetic variations correlated with a pathology that can be referred to as the genetic profile or genotype (specification as filed, page 9, lines 20-29).

The specification provides considerable teachings and guidance to the skilled person for detection of SNPs, which can be identified by finding a difference in the nucleotide sequence of an individual compared to the most common nucleotide sequence of the overall population (specification as filed, page 10, lines 17-20). The specification describes and provides patent citations for methods for SNP identification that are well known in the art, including hybridization stability methods such as SSCP, where the hybrids are identified, for example, by electrophoretic analysis, denaturing HPLC or addressable DNA array hybridization (specification as filed, page 10, lines 17-26). The specification discloses that a perturbation resulting from the hybrid instability can be exploited to detect SNPs by its impact on enzymatic reactions such as restriction endonucleases (RFLP), allele-specific oligonucleotide ligation, allele-specific cleavage,

allele-specific PCR, and allele-specific LCR (specification as filed, page 10, line 26, to page 11, line 2). In addition, other methods for detecting SNP genetic variations including use polymerase-dependent primer extension techniques such as GBA which uses single nucleotide extension or limited extension from a specific primer for analysis by, for example, mass spectrometry are set forth in the specification , which also teaches that correlation of data to identify a site of a genetic variation such as a SNP can be carried out by sequence comparison of the results of the taught assays for multiple individuals and provides several citations to the skilled person that provide further guidance on methods for sequence comparison (specification as filed, page 11, lines 2-13).

With regard to establishing a correlation, the specification teaches that certain genetic variations are correlated with a pathology or treatment of a pathology, for example, the SNP encoding the change from normal hemoglobin to sickle hemoglobin in sickle cell anemia (specification as filed, page 11, lines 13-17). The specification further discloses that methods for using a variety of patient determinants such as genetic variations to establish if one or more determinants are correlated with a pathology, or if one or more determinants are correlated with treatment of a pathology, are known in the art and provides a number of citations to patents and international patent publications that are incorporated by reference for their teachings with regard to establishing such correlations (specification as filed, page 11, lines 17-24).

The specification teaches that a compound of the invention can modulate the activity of a target molecule that plays a role in the symptoms, etiology, complications or treatment of a pathology as well as can modulate the activity of a target-protein associated with one or more genetic variations that plays a role in the symptoms, etiology, complications or treatment of a pathology (specification as filed, page 7, lines 9-14). The specification further discloses as an example a protease normally having a glutamate at a position near the active site that can have increased proteolytic activity as a result of a single nucleotide polymorphism arising in which the glutamate is changed to alanine, resulting in a particular SNP playing a role in a pathology caused by increased proteolytic activity (specification as filed, page 7, lines 17-24). A compound, such as a

protease inhibitor, can be effective against a protease target protease with this SNP by inhibiting the proteolytic activity of the protease. Armed with the guidance provided by the specification, the skilled person would have been able to prepare a composition encompassing at least two compounds, for example protease inhibitors, after confirming via routine methods, not requiring undue experimentation, that each compound modulates the activity of a target molecule, for example a protease, that is associated with one or more SNPs.

In addition to the teachings and guidance provided by the specification with regard to identifying a SNP in a target molecule, identifying a compound that modulates the activity of a target molecule associated with one or more SNPs, and establishing a correlation between a pathology or treatment thereof and a genetic variation, the specification discloses an algorithm for determining the efficacy and/or toxicity of a combination of two or more compounds for a population of patients having a pathology (specification, page 33, line 22, to page 34, line 10). Further with regard to determining efficacies, the specification exemplifies optimization of efficacy for five compounds with additive efficacies for five equally populated as well as for two compounds with additive efficacies for two variably populated genotypes (specification, Examples I and II, pages 36-44). Thus, the specification exemplifies determination and optimization of efficacy for a composition of the invention, teaching the skilled person both how to make and how to use the claimed compositions.

In view of the above, Applicant submits that the specification provides sufficient teachings to enable those in the art to can make and use the invention compositions without undue experimentation. Accordingly, Applicant respectfully requests withdrawal of the objection to the specification and corresponding rejection of claims 1-27 under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification so as to enable one skilled in the art to practice the claimed invention.

Rejections under 35 U.S.C. § 112, second paragraph

The rejection of claim 1-27 under 35 U.S.C.§ 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicant respectfully submits that each of the terms, viewed by the skilled person in light of the specification and what was known in the art, is sufficiently clear and definite to meet the requirements of section 112 of the Code.

> The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, e.g., competitors of the patent owner, can determine whether or not they infringe. That determination requires a construction of the claims according to the familiar canons of claim construction.

All Dental Prodx, LLC v. Advantage Dental Prods., 309 F.3d 774, 779-80, 64 USPQ2d 1945, 1949 (Fed. Cir. 2002) (citations omitted).

The determination of whether a claim is invalid as indefinite "depends on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the specification." *See N. Am. Vaccine, Inc. v. Am. Cyanamid Co.*, 7 F.3d 1571, 1579 (1993) (citation omitted). According to the Federal Circuit, "[M]athematical precision is not required--only a reasonable degree of particularity and definiteness." *Exxon v. US*, 265 F.3d 1371, 1381; 60 U.S.P.Q.2d 1272, 1279 (Fed. Cir. 2001).

Regarding "target molecules associated with one or more SNPs"

The Office Action further maintains that claims 1-27 are indefinite over the recitation of "target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs)."

The specification clearly apprizes the skilled person that a target molecule is considered associated with a SNP if the target molecule has a measurable characteristic. The skilled person would further understand that a measurable characteristic is one that changes in correlation with the presence or absence of a SNP and can be structure,

activity, concentration, compartmentalization, secretion, and the like. In addition, the skilled person understands that the observed change can be qualitative or quantitative.

Accordingly, the phrase "target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs)" is submitted to be sufficiently clear and definite to meet the requirements of paragraph 112 when viewed by the skilled person in light of the specification. Accordingly, removal of this ground for rejection is respectfully requested.

Regarding the term "corresponding"

Claim 7 is alleged to be indefinite over the recitation of "corresponding" to describe the relationship between a target molecule and a SNP. The Office Action argues that there are no teachings in the specification which define the term "corresponding" to have the meaning set forth in the response and no definition for this term in the art. The Office Action indicates that, if term "corresponding" is intended to refer to the actual SNP or to the amino acid residue encoded by a codon containing the SNP, then the claims should be amended to reflect this concept (current Office Action, page 19, second paragraph).

Applicant respectfully submits that the term corresponding should be viewed in context of the phrase "position corresponding," which already makes clear to the skilled person that the position is the same as that of the SNP or an amino acid residue encoded by a codon that encompasses said SNP. An accepted art meaning is not a prerequisite for interpreting a claim term that has an ordinary meaning that is well understood. When viewed by the skilled person in light of the specification and what was known in the art, the phrase "position corresponding" is sufficiently clear and definite to meet the requirements of paragraph 112. Accordingly, removal of this ground for rejection is respectfully requested.

Regarding the term "modulation effects"

Claims 17 and 21 are alleged to be indefinite over the recitation of process steps in a composition claim. Applicant submits that this rejection has been rendered moot by the amendments to claims 17 and 21, which now clarify that the claims are directed to compositions and do not alter the claim scope. Accordingly, removal of this ground for rejection is respectfully requested.

Rejection under 35 U.S.C. § 102

The rejection of claims 1-27 under 35 U.S.C. §102(a) or 102 (e) as allegedly anticipated by United States Patent No. 5,846,546, to Hurwitz et al. respectfully is traversed.

The independent rejection of claims 1-27 under 35 U.S.C. §102(b) as allegedly anticipated by United States Patent No. 5,648,077, to Ostberg et al. also is respectfully traversed.

Regarding Hurwitz et al.

The Office Action asserts that Hurwitz discloses HIV vaccines that modulate the activity of target molecules containing SNPs by inducing humoral or cellular immune responses against the target molecule. The vaccines preferably contain about 10 to 100 recombinant viruses each expressing a different HIV env protein variant (EPV). Each EPV contains a point mutation present in a different strain of HIV, which the Office Action equivocates to SNPs.

When lack of novelty is based on a printed publication that is asserted to describe the same invention, a finding of anticipation requires that the publication describe all of the elements of the claims. *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1349, 48 U.S.P.Q.2d 1225, (Fed. Cir. 1998) (quoting *Shearing v. Iolab Corp.*, 975 F.2d 1541, 1544-45, 24 U.S.P.Q.2d 1133, 1136 (Fed. Cir. 1992)). To establish a *prima facie* case of

anticipation, the Examiner must show that the single reference cited as anticipatory art describes all the elements of the claimed invention.

Briefly, base claim 1 is directed to a composition of compounds effective for treating a pathology, the composition that includes a combination of at least two compounds that modulate the activity of one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs), wherein each compound modulates the activity of at least one target molecule associated with one or more SNPs, and wherein the combination is effective for at least one patient having the pathology. Base claim 20 is directed at a composition of compounds effective for treating a pathology, said composition comprising at least two compounds that modulate the activity of at least one target molecule associated with at least one SNP, wherein said combination is effective for at least one patient having said pathology.

It is improper to arrive at anticipation by reading into the prior art reference teachings that are not there. *Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1473 (Fed. Cir. 1997). An anticipating reference must describe the patented subject matter with sufficient clarity and detail to establish that the subject matter existed in the prior art and that such existence would be recognized by persons of ordinary skill in the field of the invention. *Crown Operations Int'l, Ltd. v. Solutia, Inc.*, 289 F.3d 1367, 1375 (Fed. Cir. 2002).

Applicant has previously pointed out that the vaccines described by Hurwitz et al. appear to represent the composition of compounds effective for treating a pathology, however they also appear to be representing the one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs). The Examiner's response, in essence, concedes that the vaccines of Hurwitz, which contain about 10 to 100 recombinant viruses each expressing an HIV envelope protein variant (EPV) containing a distinct point mutation, represent both the claimed combination of at least 2 compounds as well as represent the target protein comprising a SNP (current Office Action, page 21, final paragraph).

Applicant respectfully suggests that the Examiner's argument reads into Hurwitz teachings that are not present in the reference. Not only do the vaccines described by Hurwitz et al. have to represent the composition of compounds effective for treating a pathology and the one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs), the Examiner also has not clearly pointed out how the vaccines modulate themselves, indirectly or directly, according to the teachings of the specification.

The Office has not met the burden of establishing a prima facie case of anticipation. Accordingly, withdrawal of the rejection of claims 1-27 under 35 U.S.C. §102(a) or 102 (e) as allegedly anticipated by United States Patent No. 5,846,546, to Hurwitz et al. respectfully is requested.

Regarding Ostberg et al.

According to the Office Action, Ostberg et al. discloses compositions that preferably contain a cocktail of antibodies that each bind to a different HBV protein having a point mutation (current Office Action, page 23, final paragraph).

In order to anticipate, "[t]he prior art reference must also be enabling, thereby placing the allegedly disclosed matter in the possession of the public." *Key Pharms., Inc. v. Hercon Labs. Corp.*, 981 F. Supp. 299, 311 (D. Del. 1997), *aff'd*, 161 F.3d 709 (Fed. Cir. 1998). "A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipating disclosures cited as prior art are not enabled." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003). "To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipatory subject matter." *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1566 (Fed. Cir. 1996).

While the cited passages of the Ostberg et al. patent appear to speculate that a single nucleotide change "could potentially encode for a single amino acid difference" which would be responsible for changes in the epitope recognition of the antibody, it is respectfully submitted that this speculation falls short of providing an enabling reference

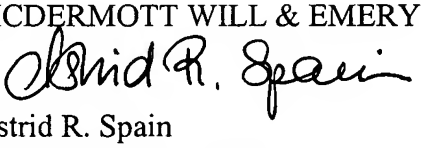
for composition of compounds effective for treating a pathology, that includes at least two compounds that modulate the activity of one or more target molecules associated with one or more Single Nucleotide Polymorphisms (SNPs), wherein each compound modulates the activity of at least one target molecule associated with one or more SNPs, and wherein the combination is effective for at least one patient having said pathology. Accordingly, withdrawal of the rejection of claims 1-27 under 35 U.S.C. §102(b) as allegedly anticipated by United States Patent No. 5,648,077, to Ostberg et al. is respectfully requested.

CONCLUSION

In light of the Remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned attorney. To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

MCDERMOTT WILL & EMERY LLP



Astrid R. Spain
Registration No. 47,956

4370 La Jolla Village Drive, Suite 700
San Diego, CA 92122
Phone: 858.535.9001 ARS:GSS
Facsimile: 858.597.1585
Date: September 19, 2005

Please recognize our Customer No. 41552 as our correspondence address.